Clean Copy of Claims, as Amended in Response to the Office Action Dated 27 August 2002

1. A method of obtaining a cell population enriched for long-term repopulating human hematopoietic stem cells (HSCs), the method comprising isolating hematopoietic cells from a human hematopoietic tissue and separating cells that express KDR on their surface (KDR^+ cells) from cells that do not express KDR on their surface using a reagent that specifically binds with KDR, thereby obtaining a KDR^+ cell population that is enriched for long-term repopulating HSCs.

2. The method of claim 1, wherein the tissue is selected from the group consisting of an embryonic tissue, a fetal tissue, and a post-natal tissue.

3. The method of claim 1, wherein the tissue is an embryonic tissue selected from the group consisting of yolk sac and liver.

4. The method of claim 1, wherein the tissue is a fetal tissue selected from the group consisting of liver, bone marrow, and peripheral blood.

5. The method of claim 1, wherein the tissue is a post-natal tissue selected from the group consisting of cord blood, bone marrow, normal peripheral blood, mobilized peripheral blood, a hepatic tissue, and a splenic tissue.

7. The method of claim 1, wherein the reagent is an antibody.

8. The method of claim 7, wherein the antibody is a monoclonal antibody.

9. The method of claim 8, wherein the monoclonal antibody is 260.4.

10. The method of claim 1, wherein the KDR^+ cells are isolated using a conjugated vascular endothelial growth factor.

11. The method of claim 1, wherein the HSCs are starvation resistant long-term repopulating human HSCs.

18. A method of preparing long-term repopulating human HSCs, the method comprising isolating hematopoietic progenitor cells (HPCs) from a human hematopoietic tissue and separating HPCs that express KDR on their surface (KDR^+ HPCs) from HPCs that do not express KDR on their surface using a reagent that specifically binds with KDR, whereby the isolated KDR^+ HPCs are enriched for long-term repopulating HSCs.

19. The method of claim 18, wherein the tissue is selected from the group consisting of an embryonic tissue, a fetal tissue, and a post-natal tissue.

20. The method of claim 18, wherein the tissue is an embryonic tissue selected from the group consisting of yolk sac and liver.

21. The method of claim 18, wherein the tissue is a fetal tissue selected from the group consisting of liver, bone marrow, and peripheral blood.

22. The method of claim 18, wherein the tissue is a post-natal tissue selected from the group consisting of cord blood, bone marrow, normal peripheral blood, mobilized peripheral blood, a hepatic tissue, and a splenic tissue.

23. The method of claim 18, further comprising isolating KDR^+ HPCs that do not express a late marker on their surface using an antibody specific for the late marker.

24. The method of claim 18, wherein the HPCs are isolated using an antibody that is specific for an early marker.

76. The method of claim 24, wherein the early marker is selected from the group consisting of CD34, Thy-1, c-kit receptor, flt3 receptor, AC133, vascular endothelial growth factor receptor I, vascular endothelial growth factor receptor III, Tie1, Tek, and basic fibroblast growth factor receptor.

26. The method of claim 76, wherein the early marker is CD34.

75. (Amended) The method of claim 18, wherein the HPCs are isolated using a method selected from the group consisting of isolating a cell based on a physical property of the cell, and isolating a cell based on a biochemical/biological property.

25. (Thrice Amended) The method of claim 18, further comprising isolating the long-term repopulating HSCs from other HPCs using one of an antibody that is specific for an early marker and an antibody that is specific for a late marker.

77. (Amended) The method of claim 18, further comprising isolating the long-term repopulating HSCs from other HPCs using an antibody that is specific for a marker selected from the group consisting of CD34, Thy-1, c-kit receptor, flt3 receptor, AC133, vascular endothelial growth factor receptor I, vascular endothelial growth factor receptor III, Tie1, Tek, basic fibroblast growth factor receptor, CD2, CD3, CD4, CD7, CD8, CD15, CD16, CD19, CD20, CD33, CD38, CD45, CD56, CD71, and glycophorin A.

78. The method of claim 77, wherein the antibody is specific for CD34.

79. The method of claim 78, wherein the long-term repopulating HSCs are isolated from other HPCs using a second antibody that is specific for a one of a late marker and an early marker other than CD34.

81. The method of claim 77, wherein the long-term repopulating HSCs are isolated from other HPCs by selecting HPCs which express an early marker selected from the group consisting of

> CD34, Thy-1, c-kit receptor, flt3 receptor, AC133, vascular endothelial growth factor receptor I, vascular endothelial growth factor receptor III, Tie1, Tek, and basic fibroblast growth factor receptor

using an antibody that is specific for the early marker.

82. (Amended) The method of claim 77, wherein the long-term repopulating HSCs are isolated from other HPCs by selecting HPCs which do not express a late marker selected from the group consisting of

> CD2, CD3, CD4, CD7, CD8, CD15, CD16, CD19, CD20, CD33, CD38, CD56, CD71, and glycophorin A

using an antibody that is specific for the late marker.

27. The method of claim 18, wherein the HPCs are isolated from the tissue using an antibody which specifically binds CD34 to select $CD34^+$ HPCs.

28. The method of claim 27, wherein the KDR^+ HPCs are isolated from the $CD34^+$ HPCs using an antibody which specifically binds KDR.

29. The method of claim 28, wherein the antibody which specifically binds KDR is a polyclonal antibody.

30. The method of claim 28, wherein the antibody which specifically binds KDR is a monoclonal antibody.

31. The method of claim 30, wherein the monoclonal antibody is 260.4.

32. The method of claim 31, wherein the KDR^+ HPCs are starvation resistant.

51. A method of expanding long-term repopulating human HSCs, the method comprising isolating HSCs that express KDR on their surface (KDR^+ HSCs) from a human hematopoietic tissue using a reagent that specifically binds with KDR and incubating the HSCs with vascular endothelial growth factor to expand the HSCs.

52. The method of claim 51, further comprising incubating the population of HSCs with another growth factor.

53. The method of claim 52, wherein the other growth factor is selected from the group consisting of flt3 ligand, kit ligand, thrombopoietin, basic fibroblast growth factor, interleukin 6, interleukin 11, interleukin 3, granulomonocytic colony-stimulatory factor, granulocytic colony-stimulatory factor, monocytic colony-stimulatory factor, erythropoietin, angiopoietin, and hepatocyte growth factor.

69. A method of isolating a stem cell capable of giving rise to at least one of a muscle cell, a hepatic oval cell, a bone cell, a cartilage cell, a fat cell, a tendon cell, and a marrow stroma cell, the method comprising isolating a hematopoietic cell that expresses KDR on its surface from a human hematopoietic tissue using a reagent that specifically binds with KDR, thereby isolating the stem cell.

71. The method of claim 69, wherein the tissue is selected from the group consisting of an embryonic tissue, a fetal tissue, and a post-natal tissue.

72. The method of claim 69, wherein the tissue is an embryonic tissue selected from the group consisting of yolk sac and liver.

73. The method of claim 69, wherein the tissue is a fetal tissue selected from the group consisting of liver, bone marrow, and peripheral blood.

74. The method of claim 69, wherein the tissue is a post-natal tissue selected from the group consisting of cord blood, bone marrow, normal peripheral blood, mobilized peripheral blood, a hepatic tissue, and a splenic tissue.

80. A method of obtaining a cell population enriched for long-term repopulating human hematopoietic stem cells (HSCs), the method comprising isolating hematopoietic cells from a human hematopoietic tissue and separating cells that express KDR on their surface but do not express a late marker on their surface from cells that either do not express KDR on their surface or express a late marker on their surface, the isolation method comprising using a reagent that specifically binds with KDR, thereby obtaining a cell population that is enriched for long-term repopulating HSCs.

83. A method of preparing long-term repopulating human HSCs, the method comprising isolating cells that express KDR on their surface and do not express a first early marker on their surface ($KDR^{+}early^{-}$ cells) using, sequentially in either order, an antibody which specifically binds with the first early marker and a reagent which specifically binds with KDR .

84. The method of claim 83, further comprising isolating the long-term repopulating HSCs from the $KDR^{+}early^{-}$ cells using an antibody which specifically binds one of a late marker and a second early marker.

85. The method of claim 83, further comprising isolating the long-term repopulating HSCs from the $KDR^{+}early^{-}$ cells by isolating cells that do not express a late marker from the $KDR^{+}early^{-}$ cells.

86. (Amended) The method of claim 85, wherein the long-term repopulating HSCs are isolated using an antibody that binds specifically with a late marker selected from the group consisting of CD2, CD3, CD4, CD7, CD8, CD15, CD16, CD19, CD20, CD33, CD38, CD56, CD71, and glycophorin A.

87. (Amended) The method of claim 85, comprising isolating $KDR^{+}early^{-}$ cells that do not express any late marker of the group consisting of

CD2, CD3, CD4, CD7, CD8, CD15, CD16, CD19, CD20, CD33, CD38, CD56, CD71, and glycophorin A

from other $KDR^{+}early^{-}$ cells.

88. The method of claim 83, wherein the first early marker is CD34.

89. The method of claim 83, wherein the long-term repopulating human HSCs are prepared by isolating $CD34^{-}$ cells from the tissue using an antibody that binds specifically with CD34, and thereafter separating $KDR^{+}CD34^{-}$ cells from other $CD34^{-}$ cells, whereby the $KDR^{+}CD34^{-}$ cells are enriched for the HSCs.

90. (Amended) The method of claim 89, further comprising separating $CD34^{-}$ cells that do not express a late marker ($CD34^{-}late^{-}$ cells) selected from the group consisting of CD2, CD3, CD4, CD7, CD8, CD15, CD16, CD19, CD20, CD33, CD38, CD56, CD71, and glycophorin A on their surface from other $CD34^{-}$ cells, whereby the $CD34^{-}late^{-}$ cells are enriched for the HSCs.

91. The method of claim 90, wherein the separation of KDR^+ and KDR^- $CD34^-$ cells is performed prior to separating $CD34^-late^-$ cells from other $CD34^-$ cells.

92. The method of claim 90, wherein the separation of KDR^+ and KDR^- $CD34^-$ cells is performed after separating $CD34^-late^-$ cells from other $CD34^-$ cells.

93. The method of claim 83, wherein the reagent is an antibody.

94. The method of claim 83, wherein the reagent is a polyclonal antibody.

95. The method of claim 83, wherein the reagent is a monoclonal antibody.

96. The method of claim 95, wherein the monoclonal antibody is 260.4.

97. (Amended) The method of claim 83, wherein $CD34^-$ $CD38^-$ cells are isolated from a human hematopoietic tissue.

98. The method of claim 97, further comprising isolating the long-term repopulating HSCs from other $CD34^-$ $CD38^-$ cells using an antibody which specifically binds one of a late marker other than CD38 and an early marker other than CD34.

99. The method of claim 83, wherein $CD34^-$ cells that do not express a late marker are isolated from the tissue.

100. (Amended) The method of claim 99, wherein the $CD34^-$ cells do not express any late marker of the group consisting of CD2, CD3, CD4, CD7, CD8, CD15, CD16, CD19, CD20, CD33, CD38, CD56, CD71, and glycophorin A.